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EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 08/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/776,252

Applicant(s)

ELLINGTON, ANDREW

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 June 2006.  
 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 29-43 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
 6) ☒ Claim(s) 29-43 is/are rejected.  
 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) ☐ All b) ☐ Some \* c) ☐ None of:  
 1. ☐ Certified copies of the priority documents have been received.  
 2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
 \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)  
 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_  
 4) ☐ Interview Summary (PTO-413)  
 Paper No(s)/Mail Date. \_\_\_\_\_  
 5) ☐ Notice of Informal Patent Application (PTO-152)  
 6) ☐ Other: \_\_\_\_\_

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## **FINAL ACTION**

### ***Status of the Claims***

1. This action is in response to papers filed 2 June 2006 in which claim 29 was amended. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 2 March 2006 are maintained based on the new matter rejection and further review of the cited art. Applicant's arguments have been thoroughly reviewed and are discussed below as they apply to the instant rejections. New grounds for rejection, necessitated by the amendments, are discussed.

Claims 29-43 are under prosecution.

### ***Claim Rejections - 35 USC § 112***

#### **New Matter**

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 29-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 29 (from which all other claims depend) has been amended to recite "not by means of a separate quenching molecule". Applicant points to numerous passages in the specification that teach two aptamers having fluorescing moieties incorporated e.g. ATP-R-Ac13

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has an acridine moiety replacing an adenosine at position 13 and DFL708 has a fluorescein molecule inserted between residues 7 and 8. While the two aptamers provided in the specification are not described as having a quenching molecule, the aptamers function as quenchers. Furthermore, neither the cited passages nor the remaining text of the specification teaches what is encompassed by the negative limitation i.e. not by means of a separate quenching molecule. For these reasons, the amendment is deemed new matter.

***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 29-37 and 40-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Gold et al (U.S. Patent No. 6,242,246, filed 15 December 1997) as defined by Pitner et al (U.S. Patent No. 5,650,275, issued 22 July 1997).

Regarding Claim 29, Gold et al disclose a method of transducing a conformational change in a signaling aptamer, the method comprising the steps of providing a signaling aptamer and by means other than a quenching molecule (reporter molecule e.g. fluorescence label, luminescent label and near IR label, Column 15, lines 49-56) covalently coupled to an

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aptamer, i.e. the labeled aptamer is prepared by methods taught by Pitner, U.S. Patent No. 5650275, Column 15, lines 44-59) wherein unbound signaling aptamer is quenched relative to the signal when aptamer undergoes a conformational change upon binding its ligand (Column 13, lines 37-59 and Fig. 5). The method further comprises, containing the signaling aptamer with the ligand for binding and detecting signal produced by the reporter (Column 13, lines 37-59 and Fig. 5). Gold et al teach the labeled signaling aptamer is prepared by methods taught by Pitner, U.S. Patent No. 5,650,275 (Column 15, lines 44-59). Pitner defines the ligand labeling as covalent (Column 5, lines 7-9). Because Gold et al teaches the signaling aptamers are labeled using the method of Pitner and because Pitner teaches the aptamer is covalently coupled to the aptamer, Gold et al anticipates the covalently coupled aptamer-reporter as claimed.

Regarding Claim 30, Gold et al disclose the method further comprising quantifying the amount of label bound to the aptamer (Column 15, lines 57-65).

Regarding Claim 31, Gold et al disclose the method wherein the optical signal is fluorescence, anisotropy, polarization, lifetime or intensity (Column 15, lines 57-65).

Regarding Claim 32, Gold et al disclose the method wherein the covalent coupling occurs during synthesis (Column 15, lines 44-47) as defined by Pitner (Column 7, lines 11-19).

Regarding Claim 33, Gold et al disclose the method wherein the reporter is a dye (e.g. Column 15, lines 52-57).

Regarding Claim 34, Gold et al disclose the method wherein the dye is a fluorescent dye (e.g. Column 15, lines 52-57).

Regarding Claim 35, Gold et al disclose the method wherein the dye is attached according to the method of Pitner (Column 15, lines 44-47) and Pitner defines the dye attachment as insertion of a fluorescein at an internal position (Column 4, lines 32-43).

Regarding Claim 36, Gold et al disclose the method wherein the dye is acridine or fluorescein (e.g. Column 15, lines 52-57).

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Regarding Claim 37, Gold et al disclose the method wherein the aptamer comprises modified or unmodified RNA or DNA (nucleic acid ligands, Column 5, lines 56-58) wherein nucleic acids are modified or unmodified RNA or DNA (Column 5, lines 23-43).

Regarding Claim 40, Gold et al disclose the method wherein the label is adjacent to a functional residue (i.e. "within the binding site of the target molecule, Column 16, lines 1-3) wherein the label is attached according to the method of Pitner (Column 15, lines 44-47) and Pitner defines the dye attachment as insertion of a fluorescein at an internal position (Column 4, lines 32-43).

Regarding Claim 42, Gold et al disclose the method wherein the aptamer is in solution i.e. the aptamer is crosslinked so that "interaction with target molecules will occur in solution" (Column 9, lines 8-12).

Regarding Claims 42-43, Gold et al disclose the method wherein the aptamer is immobilized on a chip (Column 13, lines 37-59 and Fig. 5).

#### **Response to Arguments**

6. Applicant asserts that Gold et al only teaches quenching molecules and therefore does not anticipate the instantly claimed method. The arguments has been considered but is not found persuasive because as stated above, Gold et al specifically teaches the labels include fluorescent label, luminescent label and near IR label (Column 15, lines 49-56). Furthermore, Gold et al teaches the aptamers are produced using the method of Pitner et al (Column 15, lines 46-47) who also teaches labels include fluorescent label, luminescent label and near IR label (Column 4, line 32-43).

7. Claims 29-34, 36-37 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Royer (U.S. Patent No. 5,445,935, issued 29 August 1995).

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It is noted that the Royer reference was used to reject the claims in the First Office Action on the Merits dated 29 March 2002. In the subsequent office action dated 26 November 2002, the rejection was “withdrawn as superfluous in view of the other two 102 rejections.” Hence, the record does not show that the reference is not deemed prior art against the claims.

Regarding Claim 29, Royer discloses a method of transducing a conformational change in a signaling aptamer, the method comprising the steps of providing a signaling aptamer comprising a covalently bound reporter molecule that is not a quenching molecule (fluorescent label, Column 6, lines 34-47) wherein signal from the unbound aptamer is quenched relative to the aptamer bound to the target (Column 4, line 10-47), the method comprising the steps of contacting the aptamer with the ligand and detecting the optical signal produced by the aptamer upon ligand binding (Fig. 1).

Regarding Claim 30, Royer discloses the method further comprising quantifying the amount of label bound to the aptamer (Column 4, lines 45-48).

Regarding Claim 31, Royer discloses the method wherein the optical signal is fluorescence, anisotropy, polarization (Column 7, lines 40-51).

Regarding Claim 32, Royer discloses the method wherein the covalent coupling of the reporter occurs during synthesis (Column 6, lines 34-47).

Regarding Claim 33, Royer discloses the method wherein the reporter is a dye (e.g. fluorescein Column 6, lines 63-65).

Regarding Claim 34, Royer discloses the method wherein the dye is a fluorescent dye (e.g. fluorescein Column 6, lines 63-65).

Regarding Claim 36, Royer discloses the method wherein the dye is fluorescein (e.g. Column 6, lines 63-65).

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Regarding Claim 37, Royer discloses the method wherein the aptamer comprises modified or unmodified RNA or DNA (Column 6, lines 48-50).

Regarding Claim 41, Royer discloses the method wherein the signaling aptamer is in solution (Column 9, lines 11-32).

***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold et al (U.S. Patent No. 6,242,246, filed 15 December 1997) as defined by Pitner et al (U.S. Patent No. 5,650,275, issued 22 July 1997) in view of Szostak et al. (U.S. Patent No. 5,631,146, issued 20 May 1997).

Regarding Claim 38-39, Gold et al disclose a method of transducing a conformational change in a signaling aptamer, the method comprising the steps of providing a signaling aptamer (reporter molecule covalently coupled to an aptamer, i.e. the labeled aptamer is prepared by methods taught by Pitner, U.S. Patent No. 5650275, Column 15, lines 44-59) wherein unbound signaling aptamer is quenched relative to the signal when aptamer undergoes a conformational change upon binding its ligand (Column 13, lines 37-59 and Fig. 5). The method further comprises, containing the signaling aptamer with the ligand for binding and detecting signal produced by the reporter (Column 13, lines 37-59 and Fig. 5).



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Gold et al teach their method is useful for detecting a variety of ligands for diagnosis of numerous important ligand-specific diseases (Column 7, line 48-Column 8, line 13) but they do not teach the aptamers are anti-adenosine RNA or DNA aptamer wherein the former is ATP-R-ACI3 and the latter is DFL7-8 and the ligand (target molecule) is adenosine.

However, Szostak et al teach anti-adenosine triphosphate and anti-adenosine DNA aptamers prepared by the same process (Column 4, line 56-column 6, line 9) and they further teach anti-adenosine aptamers are especially useful for ATP purification and in vivo quantification (Column 18, lines 31-42). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply anti-adenosine aptamers of Szostak et al to the target detection of Gold et al for the expected benefits of purification and in vivo quantification of an important target molecule as taught by Szostak et al (Column 18, lines 31-42).

#### **Response to Arguments**

10. Applicant asserts that Gold et al does not teach all the elements of Claim 29 and Szostak et al does not cure the deficiencies of Gold. The argument has been considered but is not found persuasive for the reasons stated above regarding Gold.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### **Conclusion**

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

  
BJ Forman, Ph.D.  
Primary Examiner  
Art Unit: 1634  
August 11, 2006